Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	8	("5959075" or "9724445" or "5668007" or "6274148").pn.	USPAT; DERWENT	ADJ	ON	2004/11/08 13:36
L2	1	"6300065".pn.	USPAT	ADJ	ON	2004/11/08 13:38
S1	571	albumin WITH fusion	USPAT	ADJ	ON	2004/10/15 17:57
S2	25	S1 SAME (erythropoeitin or insulin or hormone or calcitonin or ghrh or chemokine or leptin or (growth factor) or cytokine or somatostatin or interleukin or ghrelin)	USPAT	ADJ	ON	2004/10/15 17:56
S3	9	S1 with (stability or stable)	USPAT	ADJ	ON	2004/10/15 18:24
S4	2	("5876969" or "5766883").pn.	USPAT	ADJ	ON	2004/10/15 18:24

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  * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:39:14 ON 08 NOV 2004

=> index biosci
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
       AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS,
       BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB,
       CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 13:39:32 ON 08 NOV
2004

75 FILES IN THE FILE LIST IN STNINDEX

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=> index biosci -uspatfull
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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       BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB,
       CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 13:39:41 ON 08 NOV
2004

74 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s albumin (5A) fusion
          3   FILE ADISCTI
          8   FILE ADISINSIGHT
          2   FILE AGRICOLA
          1   FILE ANABSTR
          3   FILE BIOBUSINESS
          3   FILE BIOCOMMERCE
          7   FILE BIOENG
         89   FILE BIOSIS
         95   FILE BIOTECHABS
         95   FILE BIOTECHDS
         37   FILE BIOTECHNO
          9   FILE CABA
         18   FILE CANCERLIT
        183   FILE CAPLUS
          2   FILE CEABA-VTB
         12   FILE CIN
          5   FILE CONFSCI
         19   FILE DDFU
       8966   FILE DGENE
          4   FILE DISSABS
         19   FILE DRUGU
         43   FILE EMBASE
         30   FILE ESBIOBASE
          1   FILE FEDRIP
          1   FILE FSTA
         50   FILE GENBANK
         30   FILE IFIPAT
 42 FILES SEARCHED...
          6   FILE IMSDRUGNEWS
          8   FILE IMSRESEARCH
          3   FILE JICST-EPLUS
         23   FILE LIFESCI
         51   FILE MEDLINE
          1   FILE NIOSHTIC
          1   FILE NTIS
         25   FILE PASCAL
       2222   FILE PCTGEN
         12   FILE PHAR
          2   FILE PHARMAML
          1   FILE PHIC
         12   FILE PHIN
         42   FILE PROMT
         63   FILE SCISEARCH
         61   FILE TOXCENTER
         15   FILE USPAT2
         44   FILE WPIDS
         44   FILE WPINDEX

  46 FILES HAVE ONE OR MORE ANSWERS,    74 FILES SEARCHED IN STNINDEX

L1    QUE ALBUMIN (5A) FUSION

=> s erythropoeitin or insulin or hormone or calcitonin or ghrh or chemokine or
leptin or (growth (w) factor) or cytokine or somatostatin or interleukin or
ghrelin
      54366   FILE ADISCTI
       2804   FILE ADISINSIGHT
       5270   FILE ADISNEWS
      31368   FILE AGRICOLA
       2522   FILE ANABSTR
        255   FILE ANTE
        192   FILE AQUALINE
       8191   FILE AQUASCI
      17069   FILE BIOBUSINESS
       9083   FILE BIOCOMMERCE
      12007   FILE BIOENG
     973579   FILE BIOSIS
      29381   FILE BIOTECHABS
      29381   FILE BIOTECHDS
     237892   FILE BIOTECHNO
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      88543   FILE CABA
     236209   FILE CANCERLIT
     665966   FILE CAPLUS
       3964   FILE CEABA-VTB
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       502   FILE CEN
      8193   FILE CIN
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=> s l1 (p) (erythropoeitin or insulin or hormone or calcitonin or ghrh or
chemokine or leptin or (growth (w) factor) or cytokine or somatostatin or
interleukin or ghrelin)
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         4   FILE ADISINSIGHT
         0*  FILE ADISNEWS
         0*  FILE ANTE
         0*  FILE AQUALINE
         0*  FILE BIOCOMMERCE
         0*  FILE BIOENG
        13   FILE BIOSIS
        29*  FILE BIOTECHABS
        29*  FILE BIOTECHDS
         6*  FILE BIOTECHNO
         3   FILE CANCERLIT
        26   FILE CAPLUS
 18 FILES SEARCHED...
         0*  FILE CEABA-VTB
         3*  FILE CIN
         4   FILE CONFSCI
        10   FILE DDFU
       549   FILE DGENE
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        10   FILE DRUGU
         7   FILE EMBASE
         4*  FILE ESBIOBASE
         1*  FILE FEDRIP
         0*  FILE FOMAD
         0*  FILE FOREGE
         0*  FILE FROSTI
         0*  FILE FSTA
         6   FILE IFIPAT
 42 FILES SEARCHED...
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         5   FILE IMSRESEARCH
         0*  FILE KOSMET
         1   FILE LIFESCI
         0*  FILE MEDICONF
         6   FILE MEDLINE
         0*  FILE NTIS
         0*  FILE NUTRACEUT
         5*  FILE PASCAL
 55 FILES SEARCHED...
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         1*  FILE PHARMAML
         6   FILE PHIN
        13   FILE PROMT
        11   FILE SCISEARCH
        15   FILE TOXCENTER
         1   FILE USPAT2
         0*  FILE WATER
        15   FILE WPIDS
        15   FILE WPINDEX

 32 FILES HAVE ONE OR MORE ANSWERS,   74 FILES SEARCHED IN STNINDEX

L2   QUE L1 (P) (ERYTHROPOEITIN OR INSULIN OR HORMONE OR CALCITONIN OR GHRH OR
     CHEMOKINE OR LEPTIN OR (GROWTH (W) FACTOR) OR CYTOKINE OR SOMATOSTATIN
      OR INTERLEUKIN OR GHRELIN)

=> d rank
F1        549   DGENE
F2         29*  BIOTECHABS
F3         29*  BIOTECHDS
F4         26   CAPLUS
F5         15   TOXCENTER
F6         15   WPIDS
F7         15   WPINDEX
F8         13   BIOSIS
F9         13   PROMT
F10        11   SCISEARCH
F11        10   DDFU
F12        10   DRUGU
F13         7   EMBASE
F14         6   IFIPAT
F15         6   MEDLINE
F16         6   PHIN
F17         6*  BIOTECHNO
F18         5   IMSRESEARCH
F19         5   PHAR
F20         5*  PASCAL
F21         4   ADISINSIGHT
F22         4   CONFSCI
F23         4*  ESBIOBASE
F24         3   CANCERLIT
F25         3*  CIN
F26         1   ADISCTI
F27         1   DISSABS
F28         1   IMSDRUGNEWS
F29         1   LIFESCI
F30         1   USPAT2
F31         1*  FEDRIP
F32         1*  PHARMAML


=> file f2-f16
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY     SESSION
FULL ESTIMATED COST                               5.13        5.91

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=> s l2
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L1 (P) '
   9 FILES SEARCHED...
L3          157 L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4           93 DUP REM L3 (64 DUPLICATES REMOVED)

=> s l4 and (stability or stable)
L5           17 L4 AND (STABILITY OR STABLE)

=> d l5 bib ab 1-17

L5    ANSWER 1 OF 17  BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
AN    2004-06841  BIOTECHDS
TI    Novel fusion polypeptide having epidermal   ***growth***     ***factor***
      and human serum albumin linked to C-terminal or N-terminal of epidermal
        ***growth***     ***factor***   in which   ***stability***   of
        ***growth***     ***factor***   is enhanced by human serum albumin;
        vector-mediated fusion gene transfer and expression in host cell for
        recombinant protein production and cosmetic manufacture

AU    LEE S; YOO J; PARK S
PA    NEXGEN BIOTECHNOLOGIES INC
PI    WO 2004005340 15 Jan 2004
AI    WO 2003-KR1309 2 Jul 2003
PRAI  KR 2002-38165 3 Jul 2002; KR 2002-38165 3 Jul 2002
DT    Patent
LA    English
OS    WPI: 2004-099372 [10]
AB    DERWENT ABSTRACT:
      NOVELTY - A fusion polypeptide (I) comprising epidermal   ***growth***
        ***factor***   (EGF) and human serum albumin linked to the C-terminal or
      N-terminal of the EGF, and in which the   ***stability***   of the EGF is
      enhanced by virtue of the human serum albumin, is new.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
      following: (1) a nucleotide sequence (II) encoding a fusion polypeptide
      comprising EGF and human serum albumin linked to the C-terminal or
      N-terminal of the EGF; (2) an expression vector (III) comprising (II) and
      a promoter operably linked to the nucleotide sequence; (3) a transformant
      (IV) comprising (III); (4) preparing (I); (5) a cosmetic composition for
      skin care, which comprises a fusion polypeptide comprising EGF and human
      serum albumin linked to the C-terminal or N-terminal of the EGF as an
      active ingredient and a carrier; and (6) a pharmaceutical composition
      (P1), comprising a fusion polypeptide comprising EGF and human serum
      albumin linked to the C-terminal or N-terminal of the EGF as an active
      ingredient and a carrier.
          BIOTECHNOLOGY - Preparation: Preparing (I) involves culturing (IV)
      under conditions for expression and recovering (I) (claimed). Preferred
      Polypeptide: In (I), the human serum albumin is linked to C-terminal of
      EGF. Preferred Nucleotide: In (II), a nucleotide sequence coding for the
      human serum albumin is linked to the 3' end of the EGF. The nucleotide
      sequence coding for EGF comprises a sequence (S1) of 159 nucleotides,
      given in the specifications. Preferred Vector: In (III), a nucleotide
      sequence of EGF comprises (S1). Preferred Transformant: (IV) is a
      bacterium, fungus, plant cell or animal cell.
          USE - (I) is useful for preparing cosmetic composition for skin
      care.
          ADMINISTRATION - (I) is administered through oral, parenteral or
      topical route. Dosage ranges from 0.001-100 mg/kg.
          ADVANTAGE - (I) has higher   ***stability***   and purity.
          EXAMPLE - To amplify the epidermal   ***growth***     ***factor***
      (EGF) gene, PCR amplification was performed using the EGF gene as
      template and a pair of primers designed to introduce BamHI and HindIII
      recognition sites into 5'- and 3'- termini of the gene, respectively. The
      nucleotide sequences of primers are: reverse primer 5'-
      CCCAAGCTTTCAGCGCAGTTCCCACCACTT-3' and forward primer 5'-
      CGGGATCCAACAGCGATTCAGAATGTCCAC-3'. The PCR product was digested with
      BamHI and HindIII and extracted. The EGF gene extracted and purified was
      ligated to pUC18 and digested with BamHI and HindIII using T4 DNA ligase.
      The resulting vector was transformed into CaCl2-treated Escherichia coli
      DH5alpha and then the transformed cells with ampicillin resistance were
      selected by culturing in Luria Broth (LB) medium containing ampicillin
      (100 mg/ml). The cloned plasmids (EGF/pUC18) were isolated from the
      transformed cells. PCR amplification was performed using cDNA of human
      serum albumin as template and a pair of primers designed to introduce
      EcoRI and BamHI recognition sites into 5'- and 3'- termini of the gene,
      respectively. The nucleotide sequences of primers are: reverse primer
      5'-CGGGATCCACCGGTACGCGTAGAATCGAGACC-3' and forward primer
```

5'-CGGAATTCATGAAGTGGGTAACCTTTATTTCC-3'. The PCR product was digested with EcoRI and BamHI and extracted. The human serum albumin gene extracted and purified was ligated to EGF/pUC18 digested with EcoRI and BamHI using T4 DNA ligase. The resulting plasmid was introduced into CaCl2-treated E. coli DH5alpha and then the transformed cells with ampicillin resistance were selected by culturing in LB medium containing ampicillin (100 mg/ml). The cloned plasmids (Albumin-EGF/pUC18) were isolated from the transformed cells. Following the digestion of Albumin-EGF/pUC18 plasmid with EcoRI and HindIII, the resultant was subjected to electrophoresis on agarose gel and the ***albumin*** -EGF ***fusion*** gene was extracted and purified.(57 pages)

L5 ANSWER 2 OF 17 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
AN 2004-06830 BIOTECHDS
TI Preparing a fusion polypeptide comprising epidermal ***growth*** ***factor*** and human serum albumin in a plant comprises transforming plant cells with a polynucleotide sequence that encodes the fusion polypeptide;
vector-mediated fusion gene transfer and expression in transgenic plant for recombinant protein production and disease therapy
AU LEE S; YOO J; PARK S
PA NEXGEN BIOTECHNOLOGIES INC
PI WO 2004005520 15 Jan 2004
AI WO 2003-KR1310 2 Jul 2003
PRAI KR 2002-38165 3 Jul 2002; KR 2002-38165 3 Jul 2002
DT Patent
LA English
OS WPI: 2004-091372 [09]
AB DERWENT ABSTRACT:
NOVELTY - Preparing a fusion polypeptide comprising epidermal ***growth*** ***factor*** (EGF) and human serum albumin in a plant comprising transforming plant cells with a polynucleotide sequence comprising a sequence that encodes the fusion polypeptide, a promoter, and a 3'-non-translated region, is new.

DETAILED DESCRIPTION - Preparing a fusion polypeptide comprising epidermal ***growth*** ***factor*** (EGF) and human serum albumin in a plant comprising transforming plant cells with a polynucleotide sequence comprising a sequence that encodes the fusion polypeptide, a promoter, and a 3'-non-translated region, comprising: (a) transforming plant cells with a polynucleotide sequence comprising a nucleotide sequence encoding the fusion polypeptide comprising EGF and human serum albumin linked to the C-terminal or N-terminal of the EGF, where the ***stability*** of the EGF is enhanced by virtue of the human serum albumin; a promoter that functions in plant cells to cause the production of an RNA molecule operably linked to the nucleotide sequence; and a 3'-non-translated region that functions in plant cells to cause the polyadenylation of the 3'-end of the RNA molecule; (b) selecting transformed plant cells; (c) regenerating a plant from the transformed cells; and (d) recovering the fusion polypeptide from the regenerated plant.

WIDER DISCLOSURE - The following are also disclosed as new: (1) a nucleotide sequence encoding the fusion polypeptide; (2) an expression vector comprising the nucleotide sequence; (3) a cosmetic composition for skin care; and (4) a pharmaceutical composition.

BIOTECHNOLOGY - Preferred Plant: In preparing a fusion polypeptide, the plant is Nicotiana tabacum, Cucumis melo, Cucumis sativa, Citrullus vulgaris, or Brassica campestris. Preferred Nucleic Acid: The nucleotide sequence of the EGF comprises nucleotide 1-159 of a sequence of 165 amino acids fully defined in the specification. Preferred ***Fusion*** Protein: The human serum ***albumin*** is linked to the C-terminal of the EGF. Preferred Method: The method alternatively comprises: (a) inoculating an explant material from the plant with Agrobacterium tumifaciens harboring a vector that is capable of inserting into a genome of cell from the plant and containing the nucleotide sequence cited above; (b) regenerating the inoculated explant material on a regeneration medium to obtain regenerated shoots; (c) culturing the regenerated shoots on a rooting medium to obtain a transformed plant, where the transformed plant is capable of expressing the nucleotide sequence; and (d) recovering the fusion polypeptide from the transformed plant.

ACTIVITY - Gastrointestinal-Gen.; Antiulcer; Antiparkinsonian; Dermatological; Vulnerary. No biological data given.

MECHANISM OF ACTION - Protein Therapy. No biological data given.

USE - The method is useful for preparing a fusion polypeptide comprising epidermal ***growth*** ***factor*** and human serum ***albumin*** in plant (claimed). The ***fusion*** polypeptide is useful for preparing a cosmetic composition for skin care, and a pharmaceutical composition for treating, e.g. gastric ulcers, neurodegenerative disorders such as Parkinson's disease and wound healing.

ADMINISTRATION - Dosage is 0.001-100 mg/kg. Administration is oral, parenteral or topical.

EXAMPLE - Escherichia coli BL21 (DE3) transformed with Albumin-EGF/pET28alpha was cultured to OD650 0.5 in 5 liter fermenter and the expression of the fused gene was then induced by addition of 0.5 mM IPTG. Following additional culture for 5-6 hours, the cells were collected by centrifugation. The collected cells were completely suspended in 40 ml of buffer, disrupted by ultrasonification, centrifuged and the resulting supernatant was then collected. The supernatant was electrophoresed pm 8 % polyacrylamide gel to verify the expression of the fusion protein. The supernatant was applied to Ni-agarose column activated with a binding buffer and passed at a rate of 1-3 ml/minute. Then, using the binding buffer, the column was washed and each of 20, 40, 60, 100, 300 and 500 nM imidazole solutions was applied to the column in stepwise manner, finally eluting the fusion protein. (57 pages)

L5 ANSWER 3 OF 17 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
AN 2003-08682 BIOTECHDS
TI Novel human ***chemokine*** beta1 protein comprising deletion in amino acids from amino and/or carboxy terminus, and is a ***fusion*** protein further comprising human serum ***albumin*** , is useful for treating multiple sclerosis, asthma;
vector-mediated recombinant protein gene transfer and expression in host cell for use in gene therapy
AU BELL A; RUBEN S M
PA HUMAN GENOME SCI INC
PI WO 2002097038 5 Dec 2002
AI WO 2002-US16525 24 May 2002
PRAI US 2001-293212 25 May 2001; US 2001-293212 25 May 2001
DT Patent
LA English
OS WPI: 2003-140456 [13]
AB DERWENT ABSTRACT:
NOVELTY - A human ***chemokine*** beta1 (CKb1) protein (I) comprising a deletion in amino acid residues from amino terminus and/or carboxy

terminus of a polypeptide having a 92 residue amino acid sequence (S1), given in the specification, is new.

WIDER DISCLOSURE - (1) full-length Ckb1 polypeptides, and its analogs or derivatives; (2) isolated nucleic acid molecules encoding (I), or the full-length Ckb1 polypeptides, and their antisense analogs; (3) antibodies against (I); (4) polynucleotides encoding Ckb1 polypeptide which is a fusion polypeptide further comprising the human serum albumin (HSA), expression vectors and host cells comprising the polynucleotides; (5) Ckb1 polypeptides or Ckb1 fusion proteins coupled to a detectable label; therapeutic or cytotoxic moiety; or a radioactive material; (6) antibodies that inhibit or abolish the binding of a CCR5 ligand, polynucleotides encoding the antibodies, methods of producing the antibodies, use of the antibodies in diagnostics or therapeutics, and use of the polynucleotides encoding the antibodies in gene therapy; (7) pharmaceutical preparations comprising the Ckb1 fusion proteins; (8) transgenic organisms modified to contain the above mentioned nucleic acid molecules; (9) polypeptides containing at least 80, preferably 99 % identity to a Ckb1 protein or Ckb1 fusion protein, and nucleic acids encoding these variants, fragments of the proteins; (10) polypeptides encoded by polynucleotides which hybridize to the complement of a nucleic acid molecule encoding the above mentioned amino acid sequences; (11) diagnostic kits comprising the antibodies; (12) primary, secondary, and immortalized host cells vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g. the coding sequence corresponding to a Ckb1 protein may be replaced with a Ckb1-HSA coding region; (13) chemically modified derivatives of the Ckb1-HSA fusion proteins;(14) diagnostic assays involving the polynucleotides encoding the Ckb1 proteins, or the anti-Ckb1 antibodies; (15) gene therapy techniques involving the polynucleotides encoding Ckb1 protein; and (16) binding moieties that bind to Ckb1 protein identified by screening assays involving (I)-HSA fusion proteins.

BIOTECHNOLOGY - Preparation: (I) is prepared by standard recombinant techniques. Preferred Protein: (I) is chosen from a polypeptide comprising residues 5-n, 6-n, 7-n, 8-n or 9-n, where n is any one of residues 56-74 of (S1). (I) further comprises first a heterologous protein such as human serum albumin (HSA). The HSA is at the N- or C-terminus of Ckb1. (I) further comprises a second heterologous protein at the N-terminus of Ckb1. The second heterologous protein is 4 amino acids in length and is selective for CCR5.

ACTIVITY - Anti-HIV; Neuroprotective; Antithyroid; Antiarthritic; Antirheumatic; Immunosuppressive; Nootropic; Antiinflammatory; Antiasthmatic; Antiallergic; Osteopathic; Nephrotrophic; Tuberculostatic; Virucide; Antiatherosclerotic; Antimicrobial.

MECHANISM OF ACTION - HIV replication inhibitor; CCR5 agonist or antagonist; Upregulates or downregulates CCR5 expression. The ability of Ckb1(G28-N93):human serum albumin (HSA) was determined as follows. Ckb1(G28-N93):HSA was solubilized in phosphate buffered saline (PBS) to a concentration of 4.4 mg/ml. Human immunodeficiency virus (HIV) strain Ba-L was obtained and grown exclusively in monocytes/macrophages. Peripheral blood monocytes were isolated from HIV-1 negative donors and then cultured for 6 days, allowing maturation of the cells to a macrophage-like phenotype. At day 6, the cultures were washed 3 times to remove any non-adherent cells and serially diluted test compounds were added. The compounds and cells were incubated at 37 degrees C for 60 minutes, and then a pre-titered amount of HIV-1 Ba-L virus added. The amount of virus to be used in the assays was determined by endpoint titration with and without azidothymidine (AZT). A volume of virus (titer) was selected which provides an inhibitory concentration of 50 % between 1 and 10 nm for AZT and greater than 500 pg/ml p24 by enzyme linked immunosorbent assay (ELISA) in virus control microtiter wells. Cultures were washed a final time by media removal 24 hours post-infection, fresh compound added and the culture continued for an additional 6 days. HIV p24 content was determined by ELISA to assess virus replication. cytotoxicity by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) dye reduction was performed on day 6 of the infection. AZT, HIV-1 reverse nucleoside transcriptase inhibitor was assayed in parallel as a positive control. Results showed that Ckb1(G28-N93):HSA inhibited HIV-1 replication with an IC50 of 1.6 mg/ml and no apparent cellular toxicity at 100 mg/ml. The positive control compound AZT provided an IC50 of 2.0 nM.

USE - (I) is useful for preventing infection, preferably viral (human immunodeficiency virus (HIV)) infection, in a cell, by contacting the cell with (I). (I) is also useful for treating a disease, such as HIV infection or immune disorders, hematopoietic disorders, autoimmune disorders, multiple sclerosis, Grave's disease, arthritis, rheumatoid arthritis, transplant rejection, neurodegenerative disorders, Alzheimer's disease, inflammatory disease, asthma, allergic disorders, inflammatory bowel disease, ostecarthritis, colitis, inflammatory kidney diseases, glomerulonephritis, infectious disease, tuberculosis, hepatitis infections, herpes viral infection, viral infection, proliferative disorders or atherosclerosis, in an individual (claimed). (I) inhibits or abolishes the ability of HIV to bind to, enter into/fuse with (infect), and/or replicate in CCR5 expressing cells. (I) also acts a CCR5 agonists or antagonists, stimulate chemotaxis of CCR5-expressing cells, inhibit CCR5 ligand binding to a CCR5 molecule, or upregulate or downregulate CCR5 expression. (I) is useful as an immunological probe for the differential identification of the tissues or cell-types. (I)-HSA fusion proteins are useful for diagnosing, treating and preventing various disorders in mammals, preferably in humans. (I)-HSA fusion proteins are also useful as molecular weight markers on sodium dodecyl sulfate polyacrylamide gel electrophoresis techniques, for raising antibodies, and to test the biological activities of the Ckb1 protein. (I)-HSA fusion proteins are useful for screening for molecules that bind to the Ckb1 protein portion of the fusion protein. The fusion proteins are also useful in drug screening techniques.

ADMINISTRATION - (I)-human serum ***albumin*** (HSA) ***fusion*** protein is administered orally, parenterally, rectally, intracisternally, intravaginally, intraperitoneally, etc. Dosages of the fusion proteins administered parenterally range from 1 micro-g-10 mg/kg/day, most preferably for humans ranges from 0.01-1 mg/kg/day.

ADVANTAGE - The Ckb1 fusion proteins have increased ***stability*** , prolonged shelf-life and increased activity. The proteins exhibit selective binding to CCR5.

EXAMPLE - Vectors pScNHSA (ATCC Deposit No. PTA-3279) and pScCHSA (ATCC deposit No. PTA-3276) which are derivatives of pPPC0005 (ATCC Deposit No. PTA-3278) were used as cloning vectors into which polynucleotides encoding a ***chemokine*** beta1 (Ckb1) protein was inserted adjacent to and in translation frame with polynucleotides encoding human serum albumin (HSA). pScCHSA was used for generating Ckb1 protein-HSA fusions, while pScNHSA was used to generated HSA-Ckb1 protein fusions. Generation of pScCHSA was carried out as follows. The nucleic acid sequence encoding chimeric HSA signal peptide in pPc0005 was altered to include the XhoI and ClaI restriction sites. The XhoI and ClaI sites

inherent to pPPC00005 (located 3' of the ADH1 terminator sequence) were eliminated. Then the XhoI and ClaI restriction sites were engineered into the nucleic acid sequence that encodes the signal peptide of HAS (a chimera of the HSA leader and a kex2 site from mating factor alpha, MAF) in pPPC0006 using two rounds of polymerase chain reaction (PCR). The resulting PCR product was then purified and digested with AflII and XbaI and ligated into the same sites in pPPC0006 creating pScCHSA. The presence of the XhoI site creates a single amino acid change in the end of the signal sequence from LDKR to LEKR. The D to E change will not be present in the final ***albumin*** ***fusion*** protein expression plasmid when a nucleic acid sequence comprising a polynucleotide encoding the Ckb1 portion of the ***albumin*** ***fusion*** protein with a 5' SalI site (which is compatible with the XhoI site) and a 3' ClaI site was ligated into the XhoI and ClaI sites of pScCHSA. Ligation of SalI to XhoI restores the original amino acid sequence of the signal peptide sequence. The pScCHSA was used as cloning vectors into which polynucleotides encoding a Ckb1 protein or fragment or variant was inserted adjacent to polynucleotides encoding mature HSA. pScCHSA was used for generating Ckb1-HSA fusions. DNA encoding a Ckb1 protein was PCR amplified. Once the PCR product was obtained it was cut with Bsu36I and one of (AscI, FseI, or PmeI) and ligated into pScNHSA. The presence of the XhoI site in the HSA chimeric leader sequence created a single amino acid change in the end of the chimeric signal sequence, i.e. the HSA-kex2 signal sequence, from LDKR to LEKR. An expression vector compatible with yeast expression was transformed into yeast Saccharomyces cerevisiae individual transformants were grown for 3 days at 30 degrees C in 10 mL YEPD (1 % w/v yeast extract, 2 % w/v, peptone, 2 % w/v, dextrose), and cells were collected at stationary phase after 60 hours of growth. supernatants were collected by clarifying cells. The protein expressed was isolated and then purified. (423 pages)

L5 ANSWER 4 OF 17 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
AN 1986-11571 BIOTECHDS
TI Monoclonal antibodies against GA13-imide recognize the endogenous plant growth regulator, GA4, and related gibberellins; construction of a hybridoma secreting monoclonal antibody; application to gibberellin analysis by affinity chromatography etc.
AU Eberle J; Yamaguchi I; Nakagawa R; Takahashi N; *Weiler E W
LO Pflanzenphysiologie, Fachbereich 5, Universitaet Osnabrueck, Postfach 4469, D 4500 Osnabrueck, Germany.
SO FEBS Lett.; (1986) 202, 1, 27-31
CODEN: FEBLAL
DT Journal
LA English
AB A new approach which allows the production of gibberellin (GA)-specific monoclonal antibodies of high affinity which are useful for GA immunoassay, immunoaffinity chromatography and the generation of anti-idiotypic antibodies is reported. Female 6-8 wk old BALB/c mice were injected with bovine serum albumin-conjugated GA13-19,20-imide-beta-alanine 7-methyl ester. Similar immunizations were performed using GA1- and GA3-(C-7)-bovine serum albumin and GA3-3-succinoyl-bovine serum ***albumin*** . 4 Days prior to ***fusion*** , a final booster immunization was given. Fusions were performed with spleen cells of immunized mice and cells of the myeloma line X63.Ag8.653. Cell growth was seen 14 days after fusion, and the presence of GA-specific antibodies was monitored using RIA. Positive cell populations were purified by recloning by limiting dilution. 2 ***Stable*** hybridomas secreting antibodies of the IgG1 subclass were obtained which exhibited high affinities for GA4 methyl ester. This allowed quantitation by HPLC-RIA of ng or sub-ng amounts of GAs A2, A3, A4, A7 and A9 as the methyl esters, in biological fluids. (10 ref)

L5 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:269854 CAPLUS
DN 140:282433
TI Fusion proteins of human serum albumin with prolonged serum half-lifes for delivery of therapeutic proteins stimulating cell proliferation
IN Yu, Zailin; Fu, Yan
PA USA
SO U.S. Pat. Appl. Publ., 65 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004063635	A1	20040401	US 2003-609346	20030626
	CN 1467224	A	20040114	CN 2002-142881	20020923
PRAI	US 2002-392948P	P	20020701		

AB ***Fusion*** proteins of human serum ***albumin*** (HSA) and proteins stimulating cell proliferation such as interleukins or lymphokines are prepd. by expression of the corresponding gene in a yeast host. The serum ***albumin*** ***fusion*** protein is more ***stable*** in serum than the therapeutic protein is alone. The fusion protein therefore also has a therapeutic index higher than that of the therapeutic protein alone and has lower toxicity and longer-lasting therapeutic effects in vivo. In addn., manufg. processes are provided for efficient, cost-effective prodn. of these recombinant proteins in yeast. Manuf. of biol. active fusion proteins of ***interleukin*** 3, erythropoietin, ***interleukin*** 11, G-CSF and GM-CSF is demonstrated.

L5 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:300832 CAPLUS
DN 138:326508
TI Albumin fusion proteins with therapeutic proteins for improved shelf-life
IN Rosen, Craig A.; Haseltine, William A.
PA Human Genome Sciences, Inc., USA
SO PCT Int. Appl., 457 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003030821	A2	20030417	WO 2002-US31794	20021004
	WO 2003030821	A3	20031211		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-327281P P 20011005

AB The present invention encompasses ***fusion*** proteins of ***albumin*** with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the shelf-life, and/or to retain the therapeutic protein's activity for extended periods of time in soln., in vitro and/or in vivo, by genetically or chem. fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin. Use of ***albumin*** ***fusion*** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the ***albumin*** ***fusion*** proteins of the invention are also encompassed by the invention, as are vectors contg. these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the ***albumin*** ***fusion*** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the ***albumin*** ***fusion*** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth ***hormone*** with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37.degree., whereas recombinant human growth ***hormone*** used as control lost its biol. activity in the first week. Although the potency of the ***albumin*** ***fusion*** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. ***stability*** results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. Comprising ***albumin*** ***fusion*** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using ***albumin*** ***fusion*** proteins of the invention.

L5 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:781112 CAPLUS
DN 135:348852
TI Albumin fusion proteins with therapeutic proteins for improved shelf-life
IN Rosen, Craig A.; Haseltine, William A.
PA Human Genome Sciences, Inc., USA
SO PCT Int. Appl., 394 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079480	A1	20011025	WO 2001-US11991	20010412
	WO 2001079480	C2	20030109		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1276856	A1	20030122	EP 2001-937179	20010412	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
US 2003125247	A1	20030703	US 2001-833041	20010412	
US 2003171267	A1	20030911	US 2001-833117	20010412	
JP 2003530852	T2	20031021	JP 2001-577463	20010412	
US 2003199043	A1	20031023	US 2001-832501	20010412	
US 2003219875	A1	20031127	US 2001-833118	20010412	
US 2004010134	A1	20040115	US 2001-833245	20010412	
PRAI US 2000-229358P	P	20000412			
US 2000-199384P	P	20000425			
US 2000-256931P	P	20001221			
WO 2001-US11991	W	20010412			

AB The present invention encompasses ***fusion*** proteins of ***albumin*** with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the shelf-life, and/or to retain the therapeutic protein's activity for extended periods of time in soln., in vitro and/or in vivo, by genetically or chem. fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin. Use of ***albumin*** ***fusion*** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the ***albumin*** ***fusion*** proteins of the invention are also encompassed by the invention, as are vectors contg. these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the ***albumin*** ***fusion*** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the ***albumin*** ***fusion*** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth ***hormone*** with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37.degree., whereas recombinant human growth ***hormone*** used as control lost its biol. activity in the first week. Although the potency of the ***albumin*** ***fusion*** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. ***stability*** results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising ***albumin*** ***fusion*** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using ***albumin*** ***fusion*** proteins of the invention.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:781079 CAPLUS
DN 135:348851
TI Albumin fusion proteins with therapeutic proteins for improved shelf-life
IN Rosen, Craig A.; Haseltine, William A.
PA Human Genome Sciences, Inc, USA
SO PCT Int. Appl., 606 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079444	A2	20011025	WO 2001-US12013	20010412
	WO 2001079444	A3	20020523		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001074809	A5	20011020	AU 2001-74809	20010412
	EP 1278544	A2	20030129	EP 2001-941457	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003125247	A1	20030703	US 2001-833041	20010412
	US 2003171267	A1	20030911	US 2001-833117	20010412
	JP 2003530847	T2	20031021	JP 2001-577428	20010412
	US 2003199043	A1	20031023	US 2001-832501	20010412
	US 2003219875	A1	20031127	US 2001-833118	20010412
	US 2004010134	A1	20040115	US 2001-833245	20010412
PRAI	US 2000-229358P	P	20000412		
	US 2000-199384P	P	20000425		
	US 2000-256931P	P	20001221		
	WO 2001-US12013	W	20010412		

AB The present invention encompasses ***fusion*** proteins of ***albumin*** with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the shelf-life, and/or to retain the therapeutic protein's activity for extended periods of time in soln., in vitro and/or in vivo, by genetically or chem. fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin. Use of ***albumin*** ***fusion*** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the ***albumin*** ***fusion*** proteins of the invention are also encompassed by the invention, as are vectors contg. these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the ***albumin*** ***fusion*** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the ***albumin*** ***fusion*** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth ***hormone*** with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37.degree., whereas recombinant human growth ***hormone*** used as control lost its biol. activity in the first week. Although the potency of the ***albumin*** ***fusion*** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. ***stability*** results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising ***albumin*** ***fusion*** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using ***albumin*** ***fusion*** proteins of the invention.

L5 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:781078 CAPLUS
DN 135:348850
TI Albumin fusion proteins with therapeutic proteins for improved shelf-life
IN Rosen, Craig A.; Haseltine, William A.
PA Human Genome Sciences, Inc., USA
SO PCT Int. Appl., 374 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079443	A2	20011025	WO 2001-US11924	20010412
	WO 2001079443	A3	20020221		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001059063	A5	20011030	AU 2001-59063	20010412
	EP 1274719	A2	20030115	EP 2001-932546	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003125247	A1	20030703	US 2001-833041	20010412
	US 2003171267	A1	20030911	US 2001-833117	20010412
	JP 2003530846	T2	20031021	JP 2001-577427	20010412
	US 2003199043	A1	20031023	US 2001-832501	20010412
	US 2003219875	A1	20031127	US 2001-833118	20010412
	US 2004010134	A1	20040115	US 2001-833245	20010412
PRAI	US 2000-229358P	P	20000412		
	US 2000-199384P	P	20000425		
	US 2000-256931P	P	20001221		

WO 2001-US11924 W 20010412

AB The present invention encompasses ***fusion*** proteins of ***albumin*** with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the shelf-life, and/or to retain the therapeutic protein's activity for extended periods of time in soln., in vitro and/or in vivo, by genetically or chem. fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin. Use of ***albumin*** ***fusion*** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the ***albumin*** ***fusion*** proteins of the invention are also encompassed by the invention, as are vectors contg. these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the ***albumin*** ***fusion*** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the ***albumin*** ***fusion*** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth ***hormone*** with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37.degree., whereas recombinant human growth ***hormone*** used as control lost its biol. activity in the first week. Although the potency of the ***albumin*** ***fusion*** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. ***stability*** results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising ***albumin*** ***fusion*** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using ***albumin*** ***fusion*** proteins of the invention.

L5 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:781077 CAPLUS
DN 135:348849
TI Albumin fusion proteins with therapeutic proteins for improved shelf-life
IN Rosen, Craig A.; Haseltine, William A.
PA Human Genome Sciences, Inc., USA
SO PCT Int. Appl., 413 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079442	A2	20011025	WO 2001-US11850	20010412
	WO 2001079442	A3	20020606		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU	2001064563	A5	20011030	AU 2001-64563	20010412
EP	1276849	A2	20030122	EP 2001-938994	20010412

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US	2003125247	A1	20030703	US 2001-833041	20010412
US	2003171267	A1	20030911	US 2001-833117	20010412
US	2003199043	A1	20031023	US 2001-832501	20010412
JP	2003531590	T2	20031028	JP 2001-577426	20010412
US	2003219875	A1	20031127	US 2001-833118	20010412
US	2004010134	A1	20040115	US 2001-833245	20010412
PRAI US	2000-229358P	P	20000412		
US	2000-199384P	P	20000425		
US	2000-256931P	P	20001221		
WO	2001-US11850	W	20010412		

AB The present invention encompasses ***fusion*** proteins of ***albumin*** with various therapeutic proteins, and in particular various antibodies. Therapeutic proteins may be stabilized to extend the shelf-life, and/or to retain the therapeutic protein's activity for extended periods of time in soln., in vitro and/or in vivo, by genetically or chem. fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin. Use of ***albumin*** ***fusion*** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the ***albumin*** ***fusion*** proteins of the invention are also encompassed by the invention, as are vectors contg. these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the ***albumin*** ***fusion*** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the ***albumin*** ***fusion*** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA).

Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth ***hormone*** with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37.degree., whereas recombinant human growth ***hormone*** used as control lost its biol. activity in the first week. Although the potency of the ***albumin*** ***fusion*** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. ***stability*** results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising ***albumin*** ***fusion*** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using ***albumin*** ***fusion*** proteins of the invention.

L5 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:763025 CAPLUS
DN 135:335111

TI Albumin fusion proteins with therapeutic proteins for improved shelf-life
IN Rosen, Craig A.; Haseltine, William A.
PA Human Genome Sciences, Inc., USA
SO PCT Int. Appl., 2102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077137	A1	20011018	WO 2001-US11988	20010412
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1276756	A1	20030122	EP 2001-944114	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003125247	A1	20030703	US 2001-833041	20010412
	US 2003171267	A1	20030911	US 2001-833117	20010412
	US 2003199043	A1	20031023	US 2001-832501	20010412
	US 2003219875	A1	20031127	US 2001-833118	20010412
	US 2004010134	A1	20040115	US 2001-833245	20010412
	JP 2004506407	T2	20040304	JP 2001-575607	20010412
PRAI	US 2000-229358P	P	20000412		
	US 2000-199384P	P	20000425		
	US 2000-256931P	P	20001221		
	WO 2001-US11988	W	20010412		

AB The present invention encompasses ***fusion*** proteins of ***albumin*** with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the shelf-life, and/or to retain the therapeutic protein's activity for extended periods of time in soln., in vitro and/or in vivo, by genetically or chem. fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin. Use of ***albumin*** ***fusion*** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the ***albumin*** ***fusion*** proteins of the invention are also encompassed by the invention, as are vectors contg. these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the ***albumin*** ***fusion*** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the ***albumin*** ***fusion*** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth ***hormone*** with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37.degree., whereas recombinant human growth ***hormone*** used as control lost its biol. activity in the first week. Although the potency of the ***albumin*** ***fusion*** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. ***stability*** results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising ***albumin*** ***fusion*** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using ***albumin*** ***fusion*** proteins of the invention.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 17 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2002-055149 [07] WPIDS
DNC C2002-015688
TI ***Stable*** plastid transformation and expression vector competent for stably transforming a plastid genome for expression of heterologous genes, e.g. insulin.
DC B04 C06 D16
IN DANIELL, H
PA (AUBU) UNIV AUBURN; (UYFL-N) UNIV CENT FLORIDA; (DANI-I) DANIELL H
CYC 96
PI WO 2001072959 A2 20011004 (200207)* EN 305
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001076813 A 20011008 (200208)
EP 1274846 A2 20030115 (200306) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2003204864 A1 20031030 (200372)
ADT WO 2001072959 A2 WO 2001-US6288 20010228; AU 2001076813 A AU 2001-76813 20010228; EP 1274846 A2 EP 2001-954572 20010228, WO 2001-US6288 20010228; US 2003204864 A1 WO 2001-US6288 20010228, US 2001-807742 20010418
FDT AU 2001076813 A Based on WO 2001072959; EP 1274846 A2 Based on WO 2001072959
PRAI US 2001-185987 20010223; US 2000-185987P 20000301;
US 2001-263424P 20010123; US 2001-263473P 20010123;
US 2001-263668P 20010123; US 2001-807742 20010418
AB WO 200172959 A UPAB: 20020306
NOVELTY - A ***stable*** plastid transformation and expression vector competent for stably transforming a plastid genome, is new.
DETAILED DESCRIPTION - A ***stable*** plastid transformation and expression vector competent for stably transforming a plastid genome, is new, which comprises an expression cassette comprising as operably linked components in the 5' to 3' direction of translation:
(a) a promoter operative in the plastid,
(b) a selectable marker sequence,
(c) a heterologous DNA sequence coding for a biopolymer-proinsulin fusion gene, a cholera toxin B-subunit-proinsulin fusion gene, a plastid DNA fragment comprising a 5'UTR sequence positioned upstream of the promoter to enhance translation of proinsulin protein, a Cry2aA2 operon

which comprises two open reading frames (ORFs) where the ORF immediately upstream of Cry2aA2 codes for a putative chaperonin, a cholera toxin B-subunit-plastid modified proinsulin (PtPris) fusion wherein its nucleotide sequence is modified such that the codons are optimized for plastid expression, cholera toxin B-subunit-mini-proinsulin (Mpris) fusion where its codons are optimized for plastid expression, a synthetic protein-base polymer (PBP) fused to a biologically active molecule, an interferon gene, a ***insulin*** -like ***growth*** ***factor*** gene, a human serum ***albumin*** (HSA) gene, or a biopolymer ***fusion*** gene,

(d) a transcription termination region functional in the plastid, and

(e) flanking, each side of the expression cassette, flanking DNA sequences which are homologous to a DNA sequence inclusive of a spacer sequence of the target plastid genome, whereby ***stable*** integration of the heterologous coding sequence into the plastid genome of the target plant is facilitated throughout homologous recombination of the flanking sequence with the homologous sequence in the target plastid genome.

INDEPENDENT CLAIMS are also included for the following:

(1) a stably transformed plant which comprises plastid stably transformed with the above vector, or the progeny or seeds of it;

(2) a process for stably transforming a higher target plant species which comprises introducing into the plastid genome of the plant the above vector; and

(3) a transformed and edible tobacco or alfalfa plant of (1);

(4) a process for recovering a biopolymer by a one step extraction and purification by using the reversible property of the biopolymer; and

(5) a process for recovery of a synthetic protein-base polymer (PBP) fused with a biologically active molecule by one step extraction and purification by using the reversible property of the biopolymer of (4).

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The vector can be used to stably transform a plant. It can be used to produce edible tobacco, or alfalfa plants (all claimed).

ADVANTAGE - By producing the heterologous genes in an edible plant, the proteins can be orally delivered to patients that require them, e.g. ***insulin*** to diabetics, without the need for injections.

Dwg.0/10

L5 ANSWER 13 OF 17 PROMT COPYRIGHT 2004 Gale Group on STN

AN 2002:264945 PROMT
TI Human Genome Sciences Presentations at the American Association for Cancer Research 93rd Annual Meeting; Antitumor Activity of TRAIL Receptor-1 Agonistic Human Monoclonal Antibody.
SO PR Newswire, (10 Apr 2002) pp. DCW00910042002.
PB PR Newswire Association, Inc.
DT Newsletter
LA English
WC 2335
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB Additional Preclinical Studies of Repifermin for the Treatment of Cancer
THIS IS THE FULL TEXT: COPYRIGHT 2002 PR Newswire Association, Inc.

L5 ANSWER 14 OF 17 PROMT COPYRIGHT 2004 Gale Group on STN

AN 2000:795696 PROMT
TI HGS GAINS PRINCIPIA'S ALBUMIN FUSION PLATFORM FOR $120 M IN STOCK.
AU Willett, Matthew
SO BIOWORLD Today, (12 Sep 2000) Vol. 11, No. 176.
PB American Health Consultants, Inc.
DT Newsletter
LA English
WC 584
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB Making therapeutics just got easier for protein and peptide leader Human Genome Sciences Inc., thanks to the fusion protein technology the Rockville, Md.-based company gets through its acquisition of Principia Pharmaceuticals.
THIS IS THE FULL TEXT: COPYRIGHT 2000 American Health Consultants, Inc.

Subscription: $1350.00 per year. Published daily (5 times a week).

L5 ANSWER 15 OF 17 PROMT COPYRIGHT 2004 Gale Group on STN

AN 2000:461430 PROMT
TI PRINCIPIA SECURES FUNDING FOR DELIVERY OF PROTEINS.(Brief Article)(Company Profile)
AU Welch, Mary
SO BIOWORLD Today, (23 Aug 1999) Vol. 10, No. 162.
PB American Health Consultants, Inc.
DT Newsletter
LA English
WC 557
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB Principia Pharmaceutical Corp. is a new company developing a technology platform that uses recombinant albumin fusion proteins to provide sustained activity and improved ***stability*** .
THIS IS THE FULL TEXT: COPYRIGHT 1999 American Health Consultants, Inc.

Subscription: $1350.00 per year. Published daily (5 times a week).

L5 ANSWER 16 OF 17 IFIPAT COPYRIGHT 2004 IFI on STN
AN 10426843 IFIPAT;IFIUDB;IFICDB
TI ALBUMIN FUSION PROTEINS
INF Prior; Christopher P., Rosemont, PA, US
Rosen; Craig A., Laytonsville, MD, US
Sadeghi; Homayoun, Doylestown, PA, US
Turner; Andrew J., Eagleville, PA, US
IN Prior Christopher P; Rosen Craig A; Sadeghi Homayoun; Turner Andrew J
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
PI US 2003171267 A1 20030911
AI US 2001-833117 20010412
PRAI US 2000-199384P 20000425 (Provisional)
US 2000-229358P 20000412 (Provisional)
US 2000-256931P 20001221 (Provisional)
FI US 2003171267 20030911
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
PARN This application claims the benefit of priority under 35 U.S.C. section 119(e) based on the following U.S. provisional applications: 60/229,358

filed on Apr. 12, 2000; 60/199,384 filed on Apr. 25, 2000; and 60/256,931 filed on Dec. 21, 2000. Each of the provisional applications is hereby incorporated by reference in its entirety.

CLMN 59

GI 15 Figure(s).

FIG. 1 depicts the extended shelf-life of an HA fusion protein in terms of the biological activity (Nb2 cell proliferation) of HA-hGH remaining after incubation in cell culture media for up to 5 weeks at 37 degrees C. Under these conditions, hGH has no observed activity by week 2.

FIG. 2 depicts the extended shelf-life of an HA fusion protein in terms of the ***stable*** biological activity (Nb2 cell proliferation) of HA-hGH remaining after incubation in cell culture media for up to 3 weeks at 4, 37, or 50 degrees C. Data is normalized to the biological activity of hGH at time zero.

FIGS. 3A and 3B compare the biological activity of HA-hGH with hGH in the Nb2 cell proliferation assay. FIG. 3A shows proliferation after 24 hours of incubation with various concentrations of hGH or the albumin fusion protein, and FIG. 3B shows proliferation after 48 hours of incubation with various concentrations of hGH or the albumin fusion protein.

FIG. 4 shows a map of a plasmid (pPPC0005) that can be used as the base vector into which polynucleotides encoding the Therapeutic proteins (including polypeptides and fragments and variants thereof) may be cloned to form HA-fusions. Plasmid Map key: PRB1p: PRB1 S. cerevisiae promoter; FL: Fusion leader sequence; rHA: cDNA encoding HA; ADH1t: ADH1 S. cerevisiae terminator; T3: T3 sequencing primer site; T7: T7 sequencing primer site; Amp R: beta-lactamase gene; ori: origin of replication. Please note that in the provisional applications to which this application claims priority, the plasmid in FIG. 4 was labeled pPPC0006, instead of pPPC0005. In addition the drawing of this plasmid did not show certain pertinent restriction sites in this vector. Thus in the present application, the drawing is labeled pPPC0005 and more restriction sites of the same vector are shown.

FIG. 5 compares the recovery of vial-stored HA-IFN solutions of various concentrations with a stock solution after 48 or 72 hours of storage.

FIG. 6 compares the activity of an HA-alpha-IFN fusion protein after administration to monkeys via IV or SC.

FIG. 7 describes the bioavailability and ***stability*** of an HAalpha-IFN fusion protein.

FIG. 8 is a map of an expression vector for the production of HA alpha-IFN.

FIG. 9 shows the location of loops in HA.

FIG. 10 is an example of the modification of an HA loop.

FIG. 11 is a representation of the HA loops.

FIG. 12 shows the HA loop IV.

FIG. 13 shows the tertiary structure of HA.

FIG. 14 shows an example of a scFv-HA fusion

FIG. 15 shows the amino acid sequence of the mature form of human albumin (SEQ ID NO: 18) and a polynucleotide encoding it (SEQ ID NO: 17).

OF 17 IFIPAT COPYRIGHT 2004 IFI on STN

AB The present invention encompasses albumin fusion proteins. Nucleic acid molecules encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Additionally the present invention encompasses pharmaceutical compositions comprising albumin fusion proteins and methods of treating, preventing, or ameliorating diseases, disordrs or conditions using albumin fusion proteins of the invention.

L5 ANSWER 17 OF 17 IFIPAT COPYRIGHT 2004 IFI on STN

AN 10360161 IFIPAT;IFIUDB;IFICDB

TI RECOMBINANT FUSION PROTEINS TO GROWTH HORMONE AND SERUM ALBUMIN; SECRETED IN YEAST; STORAGE ***STABILITY*** ; MICROBIOCIDES

INF Ballance; David James, Nottingham, GB

IN Ballance David James (GB)

PAF Unassigned

PA Unassigned Or Assigned To Individual (68000)

AG FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP, 1300 I STREET, NW, WASHINGTON, DC, 20006, US

PI US 2003104578 A1 20030605

AI US 2001-984010 20011026

RLI WO 1996-GB3164 19961219 Section 371 PCT Filing UNKNOWN
US 1998-91873 19980625 CONTINUATION

PRAI GB 1995-267332 19951230

FI US 2003104578 20030605

DT Utility; Patent Application - First Publication

FS CHEMICAL
APPLICATION

CLMN 21

GI 12 Figure(s).

FIG. 1 shows the human growth hormone cDNA sequence, encoding mature hGH;

FIG. 2 shows a restriction enzyme map of pHGH1;

FIG. 3 shows a restriction enzyme map of pBST(+) and the DNA sequence of the polylinker;

FIG. 4 shows the construction of pHGH12,

FIG. 5 shows the construction of pHGH16;

FIG. 6 shows the HSA cDNA sequence, more particularly the region encoding the mature protein;

FIG. 7 shows the construction of pHGH14;

FIG. 8 shows the construction of pHGH38;

FIG. 9 shows the construction of pHGH31;

FIG. 10 shows the construction of pHGH58 or pHGH59 (Example 7);

FIG. 11 is a scheme for constructing fusions having spacers (Example 7); and

FIG. 12 shows the results of a pharmacokinetic study showing the clearance of 125I-labelled rHA-hGH compared to that of hGH following iv injection in rats. Data are from two rats in each group, and include total radioactivity and radioactivity which could be precipitated by TCA, ie that associated with protein rather than as free 125I. The calculated clearance half-life for hGH was approximately 6 minutes, compared to approximately 60 minutes for the rHA-hGH fusion protein. See Example 3.

AB ***Fusion*** proteins of ***albumin*** and growth ***hormone*** , or fusions of variants of either, are secreted well in yeast and have increased serum and storage ***stability*** .

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(FILE 'HOME' ENTERED AT 13:39:14 ON 08 NOV 2004)

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BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB,
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            3   FILE BIOCOMMERCE
            7   FILE BIOENG
           89   FILE BIOSIS
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           95   FILE BIOTECHDS
           37   FILE BIOTECHNO
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          183   FILE CAPLUS
            2   FILE CEABA-VTB
           12   FILE CIN
            5   FILE CONFSCI
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         8966   FILE DGENE
            4   FILE DISSABS
           19   FILE DRUGU
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           30   FILE ESBIOBASE
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            1   FILE FSTA
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            6   FILE IMSDRUGNEWS
            8   FILE IMSRESEARCH
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           23   FILE LIFESCI
           51   FILE MEDLINE
            1   FILE NIOSHTIC
            1   FILE NTIS
           25   FILE PASCAL
         2222   FILE PCTGEN
           12   FILE PHAR
            2   FILE PHARMAML
            1   FILE PHIC
           12   FILE PHIN
           42   FILE PROMT
           63   FILE SCISEARCH
           61   FILE TOXCENTER
           15   FILE USPAT2
           44   FILE WPIDS
           44   FILE WPINDEX
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L5             17 S L4 AND (STABILITY OR STABLE)

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FULL ESTIMATED COST                                96.94     102.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                -4.90      -4.90

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